NEPHROLOGY – EDITORIAL

Screening for peripheral artery disease in dialysis patients: an opportunity for early disease detection and timely initiation of appropriate therapeutic measures

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Otsubo et al. [1] in this issue of *International Urology and Nephrology* report that peripheral arterial disease (PAD) is an independent predictor of mortality in hemodialysis patients. In univariate analysis, the presence of PAD was associated with a 67% increase in long-term mortality risk in patients undergoing maintenance hemodialysis compared with the absence of PAD (odds ratio [OR], 1.67; 95% confidence interval [CI], 1.18–2.28; $P = 0.004$) [1]. The relation between PAD and mortality persisted even after adjustment for age, gender, duration of dialysis, diabetes mellitus and smoking (OR, 1.575;

95% CI, 1.038–2.381; $P = 0.033$) [1]. These findings support the results of earlier studies showing that PAD is common in dialysis patients and that it is associated with increased cardiovascular morbidity and mortality rates in this population [2–4]. This Editorial discusses some additional aspects that may be of interest.

There is a strong two-way correlation between impaired renal function and PAD. A recent comprehensive review demonstrated that 27–36% of patients with PAD also have concomitant impaired renal function [5]. The presence of impaired renal function in these individuals is associated not only with higher morbidity and mortality rates but also with the occurrence of cardiovascular events (stroke, myocardial infarction, and cardiovascular death) [5]. Furthermore, impaired renal function negatively affects survival, limb salvage and graft patency rates when these individuals undergo lower extremity revascularization procedures [5]. Conversely, patients on chronic dialysis have high atherosclerosis and arteriosclerosis rates [6]; the increased arterial stiffness is responsible for the high prevalence of carotid artery stenosis, myocardial infarction, PAD, and stroke in this population [6]. PAD is an atherosclerotic occlusive disease with/without vascular calcifications in the intima of lower extremity arteries [7–9]. The symptoms of PAD include intermittent claudication, which progresses to ischemic leg pain, critical limb ischemia, and finally, tissue necrosis requiring amputation. The prevalence of PAD is high among patients

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with chronic kidney disease or end-stage renal disease [7–9]. Patients with end-stage renal disease have nearly 10-fold higher lower extremity amputation rates compared with the general population [8, 9]. Cardiovascular disease is the leading cause of death in both chronic kidney disease and peritoneal dialysis/hemodialysis patients [10]. It was recently emphasized that several vascular disease prevention measures (including smoking cessation, and control of hyperphosphatemia, body weight, and blood pressure) should be initiated to reduce cardiovascular events and mortality in this high-risk population [10]. This is the reason why dialysis patients are commonly prescribed cardiovascular medications (e.g. statins, clopidogrel, acetylsalicylic acid, beta-blockers, and angiotensin-converting enzyme [ACE] inhibitors) despite the poor level of direct evidence of benefit for some of these drugs [11]. Indeed, multicentre randomized trials have failed to show a benefit of statin therapy in dialysis patients [12, 13], thus suggesting that cardiovascular disease in patients undergoing hemodialysis is different than in other patients [14, 15].

Otsubo et al. [1] used ankle–brachial index (ABI) to screen their patients for the presence of subclinical PAD. ABI is not only a marker of both PAD and systemic atherosclerosis but also a predictor of vascular events [16]. A recent study, however, disputed the value of ABI for the detection of PAD in dialysis patients [17]. This cross-sectional outpatient cohort study examined the prevalence of PAD among hemodialysis patients using both the ABI and duplex ultrasonography of the lower limbs arteries.

Although the specificity of ABI values for PAD was 94.8%, the sensitivity of this test was as low as 49.0% in this population. It was thus concluded that although ABI is a simple and reliable test for PAD screening in the general population, its sensitivity decreases considerably in dialysis patients [17]. Another recent study assessed the value of vascular calcification scores on plain radiographs of the lower limb arteries for the prediction of PAD in 102 patients with chronic kidney disease (24 pre-dialysis, 58 hemodialysis, and 20 peritoneal dialysis individuals) [7]. Patients with high vascular calcification scores demonstrated more atherosclerotic calcified plaques in the femoral and popliteal arteries. Furthermore, the prevalence of PAD in these patients was strongly associated

with high vascular calcification scores ($P < 0.01$). The conclusion reached was that a high vascular calcification score was a strong predictor for the presence of PAD (OR, 6.66; $P < 0.001$) [7]. Thus, in dialysis patients, high vascular calcification scores on plain radiographs [7] or duplex ultrasonography of the lower limb arteries [17] may be more accurate predictors of PAD than the ABI. Due to the strong association between PAD and increased cardiovascular mortality rates in dialysis patients [1–4], the early detection of subclinical PAD in these patients is crucial. The early recognition of subclinical PAD will allow the timely initiation of preventive measures (e.g. statins and antiplatelet agents). Statins not only improve renal function [18, 19] but also reduce the high cardiovascular mortality and morbidity rates seen in those individuals [20].

In the last few years, a few alternative options have emerged other than the traditional in-center hemodialysis or peritoneal dialysis, such as home dialysis [21]. These alternative dialysis options may have the disadvantage of relatively infrequent medical supervision and patient follow-up. Consequently, subclinical PAD in these patients may escape diagnosis. As a result, initiation of appropriate vascular disease prevention measures (i.e. body weight reduction, smoking cessation, antiplatelet medication, and lipid-lowering treatment with statins) may not be timely implemented. The delay in the establishment of the proper diagnosis and the subsequent delay in the implementation of routine statin and antiplatelet treatment may in turn result in increased mortality and morbidity rates.

In conclusion, screening and early detection of PAD in dialysis patients is crucial and should be coupled with timely initiation of preventive measures to reduce the high cardiovascular morbidity and mortality rates seen in this population. There is recent evidence suggesting that the ABI may not be a sensitive enough test for the diagnosis of PAD in dialysis patients [17]. In these patients, duplex ultrasonography [17] or vascular calcification scores [7] of the lower extremity arteries may be required. Nephrologists should have a high index of suspicion for the early detection of PAD in dialysis patients to ensure the timely initiation of the appropriate preventive measurements for the reduction in the high cardiovascular mortality and morbidity rates seen in this population.

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